Scientific Abstract

The purpose of this Phase I study is to explore the safety and immunologic efficacy of subcutaneous injections containing increasing numbers of autologous B-Chronic Lymphocytic Leukemia (B-CLL) cells expressing human CD40 Ligand (hCD40L) with a fixed dose of autologous human IL-2 (hIL-2)-secreting B-CLL cells. Although the malignant B-CLL cells express tumor-specific peptides (including those derived from immunoglobulin molecules) and major histocompatibility complex class I antigens, they lack the capacity for co-stimulatory signaling to T cells. This contributes to their protection from host anti-tumor immunity. The current protocol proposes to generate tumor-specific immune responses in patients with B-CLL by transferring the hCD40L gene to their tumor cells *ex vivo* thereby activating their immune system through their CD40 molecules. This in turn will up-regulate co-stimulatory molecules expression on these cells and will also stimulate maturation of host antigen-presenting cells to further facilitate an anti-tumor immune response. We will transfer hCD40L using a non-viral cell transfection system based on electroporation. This system is on file with CBER as IND 9753. We will also use this system to transform cells to express hIL-2. Animal *in vivo* and human *in vitro* studies have both shown that the combination of CD40L and IL-2 produces greater anti-tumor effector T-cell function than either molecule alone. Cells will be irradiated before injection to a degree that will block their proliferation capability, without abrogating their immunostimulatory properties.